SEQUENCE LISTING

<110> APPLIED RESEARCH SYSTEMS ARS HOLDING N.V.

<120> USE OF PRION CONVERSION MODULATING AGENTS

<130> WO/845

<160> 3

<170> PatentIn version 3.1

<210> 1
<211> 4563
<212> PRT
<213> Homo sapiens

<400> 1

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Met Asp Pro Pro Arg Pro Ala Leu Leu Ala Leu Leu Ala Leu Pro Ala
1               5                   10                  15


Leu Leu Leu Leu Leu Leu Ala Gly Ala Arg Ala Glu Glu Glu Met Leu
            20                  25                  30


Glu Asn Val Ser Leu Val Cys Pro Lys Asp Ala Thr Arg Phe Lys His
            35                  40                  45


Leu Arg Lys Tyr Thr Tyr Asn Tyr Glu Ala Glu Ser Ser Ser Gly Val
    50                  55                  60


Pro Gly Thr Ala Asp Ser Arg Ser Ala Thr Arg Ile Asn Cys Lys Val
65                  70                  75                  80


Glu Leu Glu Val Pro Gln Leu Cys Ser Phe Ile Leu Lys Thr Ser Gln
                85                  90                  95


Cys Thr Leu Lys Glu Val Tyr Gly Phe Asn Pro Glu Gly Lys Ala Leu
            100                 105                 110


Leu Lys Lys Thr Lys Asn Ser Glu Glu Phe Ala Ala Ala Met Ser Arg
            115                 120                 125


Tyr Glu Leu Lys Leu Ala Ile Pro Glu Gly Lys Gln Val Phe Leu Tyr
    130                 135                 140


Pro Glu Lys Asp Glu Pro Thr Tyr Ile Leu Asn Ile Lys Arg Gly Ile
145                 150                 155                 160


Ile Ser Ala Leu Leu Val Pro Pro Glu Thr Glu Glu Ala Lys Gln Val
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                    165                 170                    175
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Leu Phe Leu Asp Thr Val Tyr Gly Asn Cys Ser Thr His Phe Thr Val
        180   185   190

Lys Thr Arg Lys Gly Asn Val Ala Thr Glu Ile Ser Thr Glu Arg Asp
      195   200   205

Leu Gly Gln Cys Asp Arg Phe Lys Pro Ile Arg Thr Gly Ile Ser Pro
210   215   220

Leu Ala Leu Ile Lys Gly Met Thr Arg Pro Leu Ser Thr Leu Ile Ser
225   230   235   240

Ser Ser Gln Ser Cys Gln Tyr Thr Leu Asp Ala Lys Arg Lys His Val
        245   250   255

Ala Glu Ala Ile Cys Lys Glu Gln His Leu Phe Leu Pro Phe Ser Tyr
        260   265   270

Asn Asn Lys Tyr Gly Met Val Ala Gln Val Thr Gln Thr Leu Lys Leu
        275   280   285

Glu Asp Thr Pro Lys Ile Asn Ser Arg Phe Phe Gly Glu Gly Thr Lys
        290   295   300

Lys Met Gly Leu Ala Phe Glu Ser Thr Lys Ser Thr Ser Pro Pro Lys
305   310   315   320

Gln Ala Glu Ala Val Leu Lys Thr Leu Gln Glu Leu Lys Lys Leu Thr
        325   330   335

Ile Ser Glu Gln Asn Ile Gln Arg Ala Asn Leu Phe Asn Lys Leu Val
        340   345   350

Thr Glu Leu Arg Gly Leu Ser Asp Glu Ala Val Thr Ser Leu Leu Pro
        355   360   365

Gln Leu Ile Glu Val Ser Ser Pro Ile Thr Leu Gln Ala Leu Val Gln
        370   375   380

Cys Gly Gln Pro Gln Cys Ser Thr His Ile Leu Gln Trp Leu Lys Arg
385   390   395   400

Val His Ala Asn Pro Leu Leu Ile Asp Val Val Thr Tyr Leu Val Ala
        405   410   415

```
Leu Ile Pro Glu Pro Ser Ala Gln Gln Leu Arg Glu Ile Phe Asn Met
        420             425             430

Ala Arg Asp Gln Arg Ser Arg Ala Thr Leu Tyr Ala Leu Ser His Ala
        435             440             445

Val Asn Asn Tyr His Lys Thr Asn Pro Thr Gly Thr Gln Glu Leu Leu
    450             455             460

Asp Ile Ala Asn Tyr Leu Met Glu Gln Ile Gln Asp Asp Cys Thr Gly
465             470             475             480

Asp Glu Asp Tyr Thr Tyr Leu Ile Leu Arg Val Ile Gly Asn Met Gly
            485             490             495

Gln Thr Met Glu Gln Leu Thr Pro Glu Leu Lys Ser Ser Ile Leu Lys
        500             505             510

Cys Val Gln Ser Thr Lys Pro Ser Leu Met Ile Gln Lys Ala Ala Ile
    515             520             525

Gln Ala Leu Arg Lys Met Glu Pro Lys Asp Lys Asp Gln Glu Val Leu
    530             535             540

Leu Gln Thr Phe Leu Asp Asp Ala Ser Pro Gly Asp Lys Arg Leu Ala
545             550             555             560

Ala Tyr Leu Met Leu Met Arg Ser Pro Ser Gln Ala Asp Ile Asn Lys
            565             570             575

Ile Val Gln Ile Leu Pro Trp Glu Gln Asn Glu Gln Val Lys Asn Phe
            580             585             590

Val Ala Ser His Ile Ala Asn Ile Leu Asn Ser Glu Glu Leu Asp Ile
    595             600             605

Gln Asp Leu Lys Lys Leu Val Lys Glu Ala Leu Lys Glu Ser Gln Leu
    610             615             620

Pro Thr Val Met Asp Phe Arg Lys Phe Ser Arg Asn Tyr Gln Leu Tyr
625             630             635             640

Lys Ser Val Ser Leu Pro Ser Leu Asp Pro Ala Ser Ala Lys Ile Glu
            645             650             655
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Gly Asn Leu Ile Phe Asp Pro Asn Asn Tyr Leu Pro Lys Glu Ser Met
        660             665             670


Leu Lys Thr Thr Leu Thr Ala Phe Gly Phe Ala Ser Ala Asp Leu Ile
        675             680             685


Glu Ile Gly Leu Glu Gly Lys Gly Phe Glu Pro Thr Leu Glu Ala Leu
    690             695             700


Phe Gly Lys Gln Gly Phe Phe Pro Asp Ser Val Asn Lys Ala Leu Tyr
705             710             715             720


Trp Val Asn Gly Gln Val Pro Asp Gly Val Ser Lys Val Leu Val Asp
            725             730             735


His Phe Gly Tyr Thr Lys Asp Asp Lys His Glu Gln Asp Met Val As n
            740             745             750


Gly Ile Met Leu Ser Val Glu Lys Leu Ile Lys Asp Leu Lys Ser Lys
        755             760             765


Glu Val Pro Glu Ala Arg Ala Tyr Leu Arg Ile Leu Gly Gl u Glu Leu
    770             775             780


Gly Phe Ala Ser Leu His Asp Leu Gln Leu Leu Gly Lys Leu Leu Leu
785             790             795             800


Met Gly Ala Arg Thr Leu Gln Gly Ile Pro Gln Me t Ile Gly Glu Val
            805             810             815


Ile Arg Lys Gly Ser Lys Asn Asp Phe Phe Leu His Tyr Ile Phe Met
        820             825             830


Glu Asn Ala Phe Glu Leu Pro Thr Gly Al a Gly Leu Gln Leu Gln Ile
        835             8'40            845


Ser Ser Ser Gly Val Ile Ala Pro Gly Ala Lys Ala Gly Val Lys Leu
    850             855             860


Glu Val Ala Asn Met Gln Ala Gl u Leu Val Ala Lys Pro Ser Val Ser
865             870             875             880


Val Glu Phe Val Thr Asn Met Gly Ile Ile Ile Pro Asp Phe Ala Arg
            885             890             895
```

Ser Gly Val Gln Met As n Thr Asn Phe Phe His Glu Ser Gly Leu Glu
        900   905   910

Ala His Val Ala Leu Lys Ala Gly Lys Leu Lys Phe Ile Ile Pro Ser
        915   920   925

Pro Lys Arg Pro Val Lys Leu Leu Ser Gly Gly Asn Thr Leu His Leu
        930   935   940

Val Ser Thr Thr Lys Thr Glu Val Ile Pro Pro Leu Ile Glu Asn Arg
945   950   955   960

Gln Ser Trp Ser Val Cys Lys Gln Val Phe Pro Gly Leu Asn Tyr Cys
                965   970   975

Thr Ser Gly Ala Tyr Ser Asn Ala Ser Ser Thr Asp Ser Ala Ser Tyr
            980   985   990

Tyr Pro Leu Thr Gly Asp Thr Arg Leu Glu Leu Glu Leu Arg Pro Thr
        995   1000   1005

Gly Glu Ile Glu Gln Tyr Ser Val Ser Ala Thr Tyr Glu Leu Gln
    1010   1015   1020

Arg Glu Asp Arg Ala Leu Val Asp Thr Leu Lys Phe Val Thr Gln
    1025   1030   1035

Ala Glu Gly Ala Lys Gln Thr Glu Ala Thr Met Thr Phe Lys Tyr
    1040   1045   1050

Asn Arg Gln Ser Met Thr Leu Ser Ser Glu Val Gln Ile Pro Asp
    1055   1060   1065

Phe Asp Val Asp Leu Gly Thr Ile Leu Arg Val Asn Asp Glu Ser
    1070   1075   1080

Thr Glu Gly Lys Thr Ser Tyr Arg Leu Thr Leu Asp Ile Gln Asn
    1085   1090   1095

Lys Lys Ile Thr Glu Val Ala Leu Met Gly His Leu Ser Cys Asp
    1100   1105   1110

Thr Lys Glu Glu Arg Lys Ile Lys Gly Val Ile Ser Ile Pro Arg
    1115   1120   1125

Leu Gln Ala Glu Ala Arg Ser Glu Ile Leu Ala His Trp Ser Pro

```
                  1130                  1135                  1140


   Ala Lys Leu Leu Leu Gln Met Asp Ser Ser Ala Thr Ala Tyr Gly
       1145                  1150                  1155


   Ser Thr Val Ser Lys Arg Val Ala Trp His Tyr Asp Glu Glu Lys
       1160                  1165                  1170


   Ile Glu Phe Glu Trp Asn Thr Gly Thr Asn Val Asp Thr Lys Lys
       1175                  1180                  1185


   Met Thr Ser Asn Phe Pro Val Asp Leu Ser Asp Tyr Pro Lys Ser
       1190                  1195                  1200


   Leu His Met Tyr Ala Asn Arg Leu Leu Asp His Arg Val Pro Glu
       1205                  1210                  1215


   Thr Asp Met Thr Phe Arg His Val Gly Ser Lys Leu Ile Val Ala
       1220                  1225                  1230


   Met Ser Ser Trp Leu Gln Lys Ala Ser Gly Ser Leu Pro Tyr Thr
       1235                  1240                  1245


   Gln Thr Leu Gln Asp His Leu Asn Ser Leu Lys Glu Phe Asn Leu
       1250                  1255                  1260


   Gln Asn Met Gly Leu Pro Asp Phe His Ile Pro Glu Asn Leu Phe
       1265                  1270                  1275


   Leu Lys Ser Asp Gly Arg Val Lys Tyr Thr Leu Asn Lys Asn Ser
       1280                  1285                  1290


   Leu Lys Ile Glu Ile Pro Leu Pro Phe Gly Gly Lys Ser Ser Arg
       1295                  1300                  1305


   Asp Leu Lys Met Leu Glu Thr Val Arg Thr Pro Ala Leu His Phe
       1310                  1315                  1320


   Lys Ser Val Gly Phe His Leu Pro Ser Arg Glu Phe Gln Val Pro
       1325                  1330                  1335


   Thr Phe Thr Ile Pro Lys Leu Tyr Gln Leu Gln Val Pro Leu Leu
       1340                  1345                  1350


   Gly Val Leu Asp Leu Ser Thr Asn Val Tyr Ser Asn Leu Tyr Asn
       1355                  1360                  1365
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Trp Ser  Ala Ser Tyr Ser Gly  Gly Asn Thr Ser Thr  Asp His Phe
    1370             1375             1380

Ser Leu  Arg Ala Arg Tyr His  Met Lys Ala Asp Ser  Val Val Asp
    1385             1390             1395

Leu Leu  Ser Tyr Asn Val Gln  Gly Ser Gly Glu Thr  Thr Tyr Asp
    1400             1405             1410

His Lys  Asn Thr Phe Thr Leu  Ser Cys Asp Gly Ser  Leu Arg His
    1415             1420             1425

Lys Phe  Leu Asp Ser Asn Ile  Lys Phe Ser His Val  Glu Lys Leu
    1430             1435             1440

Gly Asn  Asn Pro Val Ser Lys  Gly Leu Leu Ile Phe  Asp Ala Ser
    1445             1450             1455

Ser Ser  Trp Gly Pro Gln Met  Ser Ala Ser Val His  Leu Asp  Ser
    1460             1465             1470

Lys Lys  Lys Gln His Leu Phe  Val Lys Glu Val Lys  Ile Asp Gly
    1475             1480             1485

Gln Phe  Arg Val Ser Ser Phe  Tyr Ala Lys Gly Thr  Tyr  Gly Leu
    1490             1495             1500

Ser Cys  Gln Arg Asp Pro Asn  Thr Gly Arg Leu Asn  Gly Glu Ser
    1505             1510             1515

Asn Leu  Arg Phe Asn Ser Ser  Tyr Leu Gln Gly Thr   Asn Gln Ile
    1520             1525             1530

Thr Gly  Arg Tyr Glu Asp Gly  Thr Leu Ser Leu Thr  Ser Thr Ser
    1535             1540             1545

Asp Leu  Gln Ser Gly Ile Ile  Lys Asn Thr Ala  Ser  Leu Lys Tyr
    1550             1555             1560

Glu Asn  Tyr Glu Leu Thr Leu  Lys Ser Asp Thr Asn  Gly Lys Tyr
    1565             1570             1575

Lys Asn  Phe Ala Thr Ser Asn  Lys Met Asp Met Thr  Phe Ser Lys
    1580             1585             1590
```

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Gln Asn  Ala Leu Leu Arg Ser  Glu Tyr Gln Ala Asp  Tyr Glu Ser
    1595             1600             1605

Leu Arg  Phe Phe Ser Leu Leu  Ser Gly Ser Leu Asn  Ser His Gly
    1610             1615             1620

Leu Glu  Leu Asn Ala Asp Ile  Leu Gly Thr Asp Lys  Ile Asn Ser
    1625             1630             1635

Gly Ala  His Lys Ala Thr Leu  Arg Ile Gly Gln Asp  Gly Ile Ser
    1640             1645             1650

Thr Ser  Ala Thr Thr Asn Leu  Lys Cys Ser Leu Leu  Val Leu Glu
    1655             1660             1665

Asn Glu  Leu Asn Ala Glu Leu  Gly Leu Ser Gly Ala  Ser Met Lys
    1670             1675             1680

Leu Thr  Thr Asn Gly Arg Phe  Arg Glu His Asn Ala  Lys Phe Ser
    1685             1690             1695

Leu Asp  Gly Lys Ala Ala Leu  Thr Glu Leu Ser Leu  Gly Ser Ala
    1700             1705             1710

Tyr Gln  Ala Met Ile Leu Gly  Val Asp Ser Lys Asn  Ile Phe Asn
    1715             1720             1725

Phe Lys  Val Ser Gln Glu Gly  Leu Lys Leu Ser Asn  Asp Met Met
    1730             1735             1740

Gly Ser  Tyr Ala Glu Met Lys  Phe Asp His Thr Asn  Ser Leu Asn
    1745             1750             1755

Ile Ala  Gly Leu Ser Leu Asp  Phe Ser Ser Lys Leu  Asp Asn Ile
    1760             1765             1770

Tyr Ser  Ser Asp Lys Phe Tyr  Lys Gln Thr Val Asn  Leu Gln Leu
    1775             1780             1785

Gln Pro  Tyr Ser Leu Val Thr  Thr Leu Asn Ser Asp  Leu Lys Tyr
    1790             1795             1800

Asn Ala  Leu Asp Leu Thr Asn  Asn Gly Lys Leu Arg  Leu Glu Pro
    1805             1810             1815
```

Leu Lys   Leu His Val Ala Gly   Asn Leu Lys Gly Ala   Tyr Gln Asn
    1820   1825   1830

Asn Glu   Ile Lys His Ile Tyr   Ala Ile Ser Ser Ala   Ala Leu Ser
    1835   1840   1845

Ala Ser   Tyr Lys Ala Asp Thr   Val Ala Lys Val Gln   Gly Val Glu
    1850   1855   1860

Phe Ser   His Arg Leu Asn Thr   Asp Ile Ala Gly Leu   Ala Ser Ala
    1865   1870   1875

Ile Asp   Met Ser Thr Asn Tyr   Asn Ser Asp Ser Leu   His Phe Ser
    1880   1885   1890

Asn Val   Phe Arg Ser Val Met   Ala Pro Phe Thr Met   Thr Ile Asp
    1895   1900   1905

Ala His   Thr Asn Gly Asn Gly   Lys Leu Ala Leu Trp   Gly Glu His
    1910   1915   1920

Thr Gly   Gln Leu Tyr Ser Lys   Phe Leu Leu Lys Ala   Glu Pro Leu
    1925   1930   1935

Ala Phe   Thr Phe Ser His Asp   Tyr Lys Gly Ser Thr   Ser His His
    1940   1945   1950

Leu Val   Ser Arg Lys Ser Ile   Ser Ala Ala Leu Glu   His Lys Val
    1955   1960   1965

Ser Ala   Leu Leu Thr Pro Ala   Glu Gln Thr Gly Thr   Trp Lys Leu
    1970   1975   1980

Lys Thr   Gln Phe Asn Asn Asn   Glu Tyr Ser Gln Asp   Leu Asp Ala
    1985   1990   1995

Tyr Asn   Thr Lys Asp Lys Ile   Gly Val Glu Leu Thr   Gly Arg Thr
    2000   2005   2010

Leu Ala   Asp Leu Thr Leu Leu   Asp Ser Pro Ile Lys   Val Pro Leu
    2015   2020   20 25

Leu Leu   Ser Glu Pro Ile Asn   Ile Ile Asp Ala Leu   Glu Met Arg
    2030   2035   2040

Asp Ala   Val Glu Lys Pro Gln   Glu Phe Thr Ile Val   Ala Phe Val

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          2045                 2050                 2055

    Lys Tyr  Asp Lys Asn Gln Asp  Val His Ser Ile Asn  Leu Pro Phe
        2060                 2065                 2070

    Phe Glu  Thr Leu Gln Glu Tyr  Phe Glu Arg Asn Arg  Gln Thr Ile
        2075                 2080                 2085

    Ile Val  Val Val Glu Asn Val  Gln Arg Asn Leu Lys  His Ile Asn
        2090                 2095                 2100

    Ile Asp  Gln Phe Val Arg Lys  Tyr Arg Ala Ala Leu  Gly Lys Leu
        2105                 2110                 2115

    Pro Gln  Gln Ala Asn Asp Tyr  Leu Asn Ser Phe Asn  Trp Glu Arg
        2120                 2125                 2130

    Gln Val  Ser His Ala Lys Glu  Lys Leu Thr Ala Leu  Thr Lys Lys
        2135                 2140                 2145

    Tyr Arg  Ile Thr Glu Asn Asp  Ile Gln Ile Ala Leu  Asp Asp Ala
        2150                 2155                 2160

    Lys Ile  Asn Phe Asn Glu Lys  Leu Ser Gln Leu Gln  Thr Tyr Met
        2165                 217 0                2175

    Ile Gln  Phe Asp Gln Tyr Ile  Lys Asp Ser Tyr Asp  Leu His Asp
        2180                 2185                 2190

    Leu Lys  Ile Ala Ile Ala Asn  Ile Ile Asp Glu Ile  Ile Glu Lys
        2195                 2200                 2205

    Leu Lys  Ser Leu Asp Glu His  Tyr His Ile Arg Val  Asn Leu Val
        2210                 2215                 2220

    Lys Thr  Ile His Asp Leu His  Leu Phe Ile Glu Asn  Ile Asp Phe
        2225                 2230                 2235

    Asn Lys  Ser Gly Ser Ser Thr  Ala Ser Trp Ile Gln  Asn Val Asp
        2240                 2245                 2250

    Thr Lys  Tyr Gln Ile Arg Ile  Gln Ile Gln Glu Lys  Leu Gln Gln
        2255                 2260                 2265

    Leu Lys  Arg His Ile Gln Asn  Ile Asp Ile Gln His  Leu Ala Gly
        2270                 2275                 2280
```

```
Lys Leu  Lys Gln His Ile Glu  Ala Ile Asp Val Arg  Val Leu Leu
    2285                 2290                 2295


Asp Gln  Leu Gly Thr Thr Ile  Ser Phe Glu Arg Ile  Asn Asp Val
    2300                 2305                 2310


Leu Glu  His Val Lys His Phe  Val Ile Asn Leu Ile  Gly Asp Phe
    2315                 2320                 2325


Glu Val  Ala Glu Lys Ile Asn  Ala Phe Arg Ala Lys  Val His Glu
    2330                 2335                 2340


Leu Ile  Glu Arg Tyr Glu Val  Asp Gln Gln Ile Gln  Val Leu Met
    2345                 2350                 2355


Asp Lys  Leu Val Glu Leu Thr  His Gln Tyr Lys Leu  Lys Glu Thr
    2360                 2365                 2370


Ile Gln  Lys Leu Ser Asn Val  Leu Gln Gln Val Lys  Ile Lys Asp
    2375                 2380                 2385


Tyr Phe  Glu Lys Leu Val Gly  Phe Ile Asp Asp Ala  Val Lys Lys
    2390                 2395                 2400


Leu Asn  Glu Leu Ser Phe Lys  Thr Phe Ile Glu Asp  Val Asn L ys
    2405                 2410                 2415


Phe Leu  Asp Met Leu Ile Lys  Lys Leu Lys Ser Phe  Asp Tyr His
    2420                 2425                 2430


Gln Phe  Val Asp Glu Thr Asn  Asp Lys Ile Arg Glu  Val T hr Gln
    2435            .    2440                 2445


Arg Leu  Asn Gly Glu Ile Gln  Ala Leu Glu Leu Pro  Gln Lys Ala
    2450                 2455                 2460


Glu Ala  Leu Lys Leu Phe Leu  Glu Glu Thr Lys Ala  T hr Val Ala
    2465                 2470                 2475


Val Tyr  Leu Glu Ser Leu Gln  Asp Thr Lys Ile Thr  Leu Ile Ile
    2480                 2485                 2490


Asn Trp  Leu Gln Glu Ala Leu  Ser Ser Ala Ser Le u  Ala His Met
    2495                 2500                 2505
```

Lys Ala Lys Phe Arg Glu Thr Leu Glu Asp Thr Arg Asp Arg Met
    2510   2515   2520

Tyr Gln Met Asp Ile Gln Gln Glu Leu Gln Ar g Tyr Leu Ser Leu
    2525   2530   2535

Val Gly Gln Val Tyr Ser Thr Leu Val Thr Tyr Ile Ser Asp Trp
    2540   2545   2550

Trp Thr Leu Ala Ala Lys Asn Leu Thr As p Phe Ala Glu Gln Tyr
    2555   2560   2565

Ser Ile Gln Asp Trp Ala Lys Arg Met Lys Ala Leu Val Glu Gln
    2570   2575   2580

Gly Phe Thr Val Pro Glu Ile Lys Th r Ile Leu Gly Thr Met Pro
    2585   2590   2595

Ala Phe Glu Val Ser Leu Gln Ala Leu Gln Lys Ala Thr Phe Gln
    2600   2605   2610

Thr Pro Asp Phe Ile Val Pro Le u Thr Asp Leu Arg Ile Pro Ser
    2615   2620   2625

Val Gln Ile Asn Phe Lys Asp Leu Lys Asn Ile Lys Ile Pro Ser
    2630   2635   2640

Arg Phe Ser Thr Pro Glu Phe Thr Ile Leu Asn Thr Phe His Ile
    2645   2650   2655

Pro Ser Phe Thr Ile Asp Phe Val Glu Met Lys Val Lys Ile Ile
    2660   2665   2670

Arg Thr Ile Asp Gln Met Gln Asn Ser Glu Leu Gln Trp Pro Val
    2675   2680   2685

Pro Asp Ile Tyr Leu Arg Asp Leu Lys Val Glu Asp Ile Pro Leu
    2690   2695   2700

Ala Arg Ile Thr Leu Pro Asp Phe Arg Leu Pro Glu Ile Ala Ile
    2705   2710   2715

Pro Glu Phe Ile Ile Pro Thr Leu Asn Leu Asn Asp Phe Gln Val
    2720   2725   2730

Pro Asp Leu His Ile Pro Glu Phe Gln Leu Pro His Ile Ser His
    2735   2740   2745

Thr Ile Glu Val Pro Thr Phe Gly Lys Leu Tyr Ser Ile Leu Lys
    2750   2755   2760

Ile Gln Ser Pro Leu Phe Thr Leu Asp Ala Asn Ala Asp Ile Gly
    2765   2770   2775

Asn Gly Thr Thr Ser Ala Asn Glu Ala Gly Ile Ala Ala Ser Ile
    2780   2785   2790

Thr Ala Lys Gly Glu Ser Lys Leu Glu Val Leu Asn Phe Asp Phe
    2795   2800   2805

Gln Ala Asn Ala Gln Leu Ser Asn Pro Lys Ile Asn Pro Leu Ala
    2810   2815   2820

Leu Lys Glu Ser Val Lys Phe Ser Ser Lys Tyr Leu Arg Thr Glu
    2825   2830   2835

His Gly Ser Glu Met Leu Phe Phe Gly Asn Ala Ile Glu Gly Lys
    2840   2845   2850

Ser Asn Thr Val Ala Ser Leu His Thr Glu Lys Asn Thr Leu Glu
    2855   2860   2865

Leu Ser Asn Gly Val Ile Val Lys Ile Asn Asn Gln Leu Thr Leu
    2870   2875   2880

Asp Ser Asn Thr Lys Tyr Phe His Lys Leu Asn Ile Pro Lys Leu
    2885   2890   2895

Asp Phe Ser Ser Gln Ala Asp Leu Arg Asn Glu Ile Lys Thr Leu
    2900   2905   2910

Leu Lys Ala Gly His Ile Ala Trp Thr Ser Ser Gly Lys Gly Ser
    2915   2920   2925

Trp Lys Trp Ala Cys Pro Arg Phe Ser Asp Glu Gly Thr His Glu
    2930   2935   2940

Ser Gln Ile Ser Phe Thr Ile Glu Gly Pro Leu Thr Ser Phe Gly
    2945   2950   2955

Leu Ser Asn Lys Ile Asn Ser Lys His Leu Arg Val Asn Gln Asn

                2960   2965   2970

    Leu Val Tyr Glu Ser Gly Ser Leu Asn Phe Ser Lys Leu Glu Ile
        2975   2980   2985

    Gln Ser Gln Val Asp Ser Gln His Val Gly His Ser Val Leu Thr
        2990   2995   3000

    Ala Lys Gly Met Ala Leu Phe Gly Glu Gly Lys Ala Glu Phe Thr
        3005   3010   3015

    Gly Arg His Asp Ala His Leu Asn Gly Lys Val Ile Gly Thr Leu
        3020   3025   3030

    Lys Asn Ser Leu Phe Phe Ser Ala Gln Pro Phe Glu Ile Thr Ala
        3035   3040   3045

    Ser Thr Asn Asn Glu Gly Asn Leu Lys Val Arg Phe Pro Leu Arg
        3050   3055   3060

    Leu Thr Gly Lys Ile Asp Phe Leu Asn Asn Tyr Ala Leu Phe Leu
        3065   3070   3075

    Ser Pro Ser Ala Gln Gln Ala Ser Trp Gln Val Ser Ala Arg Phe
        3080   3085   3090

    Asn Gln Tyr Lys Tyr Asn Gln Asn Phe Ser Ala Gly Asn Asn Glu
        3095   3100   3105

    Asn Ile Met Glu Ala His Val Gly Ile Asn Gly Glu Ala Asn Leu
        3110   3115   3120

    Asp Phe Leu Asn Ile Pro Leu Thr Ile Pro Glu Met Arg Leu Pro
        3125   3130   3135

    Tyr Thr Ile Ile Thr Thr Pro Pro Leu Lys Asp Phe Ser Leu Trp
        3140   3 145   3150

    Glu Lys Thr Gly Leu Lys Glu Phe Leu Lys Thr Thr Lys Gln Ser
        3155   3160   3165

    Phe Asp Leu Ser Val Lys Ala Gln Tyr Lys Lys Asn Lys His Arg
        3170   3175   3180

    His Ser Ile Thr Asn Pro Leu Ala Val Leu Cys Glu Phe Ile Ser
        3185   3190   3195

```
Gln Ser  Ile Lys Ser Phe Asp  Arg His Phe Glu Lys  Asn Arg Asn
    3200             3205             3210

Asn Ala  Leu Asp Phe Val Thr  Lys Ser Tyr Asn Glu  Thr Lys Ile
    3215             3220             3225

Lys Phe  Asp Lys Tyr Lys Ala  Glu Lys Ser His Asp  Glu Leu Pro
    3230             3235             3240

Arg Thr  Phe Gln Ile Pro Gly  Tyr Thr Val Pro Val  Val Asn Val
    3245             3250             3255

Glu Val  Ser Pro Phe Thr Ile  Glu Met Ser Ala Phe  Gly Tyr Val
    3260             3265             3270

Phe Pro  Lys Ala Val Ser Met  Pro Ser Phe Ser Ile  Leu Gly Ser
    3275             3280             3285

Asp Val  Arg Val Pro Ser Tyr  Thr Leu Ile Leu Pro  Ser Leu Glu
    3290             3295             3300

Leu Pro  Val Leu His Val Pro  Arg Asn Leu Lys Leu  Ser Leu Pro
    3305             3310             3315

His Phe  Lys Glu Leu Cys Thr  Ile Ser His Ile Phe  Ile Pro Ala
    3320             3325             3330

Met Gly  Asn Ile Thr Tyr Asp  Phe Ser Phe Lys Ser  Ser Val Ile
    3335             3340             3345

Thr Leu  Asn Thr Asn Ala Glu  Leu Phe Asn Gln Ser  Asp Ile Val
    3350             3355             3360

Ala His  Leu Leu Ser Ser Ser  Ser Ser Val Ile Asp  Ala Leu Gln
    3365             3370             3375

Tyr Lys  Leu Glu Gly Thr Thr  Arg Leu Thr Arg Lys  Arg Gly Leu
    3380             3385             3390

Lys Leu  Ala Thr Ala Leu Ser  Leu Ser Asn Lys Phe  Val Glu Gly
    3395             3400             3405

Ser His  Asn Ser Thr Val Ser  Leu Thr Thr Lys Asn  Met Glu Val
    3410             3415             3420
```

Ser Val Ala Lys Thr Thr Lys Ala Glu Ile Pro Ile Leu Arg Met
    3425   3430   3435

Asn Phe Lys Gln Glu Leu Asn Gly Asn Thr Lys Ser Lys Pro Thr
    3440   3445   3450

Val Ser Ser Ser Met Glu Phe Lys Tyr Asp Phe Asn Ser Ser Met
    3455   3460   3465

Leu Tyr Ser Thr Ala Lys Gly Ala Val Asp His Lys Leu Ser Leu
    3470   3475   3480

Glu Ser Leu Thr Ser Tyr Phe Ser Ile Glu Ser Ser Thr Lys Gly
    3485   3490   3495

Asp Val Lys Gly Ser Val Leu Ser Arg Glu Tyr Ser Gly Thr Ile
    3500   3505   3510

Ala Ser Glu Ala Asn Thr Tyr Leu Asn Ser Lys Ser Thr Arg Ser
    3515   3520   3525

Ser Val Lys Leu Gln Gly Thr Ser Lys Ile Asp Asp Ile Trp Asn
    3530   3535   3540

Leu Glu Val Lys Glu Asn Phe Ala Gly Glu Ala Thr Leu Gln Arg
    3545   3550   3555

Ile Tyr Ser Leu Trp Glu His Ser Thr Lys Asn His Leu Gln Leu
    3560   3565   3570

Glu Gly Leu Phe Phe Thr Asn Gly Glu His Thr Ser Lys Ala Thr
    3575   3580   3585

Leu Glu Leu Ser Pro Trp Gln Met Ser Ala Leu Val Gln Val His
    3590   3595   3600

Ala Ser Gln Pro Ser Ser Phe His Asp Phe Pro Asp Leu Gly Gln
    3605   3610   3615

Glu Val Ala Leu Asn Ala Asn Thr Lys Asn Gln Lys Ile Arg Trp
    3620   3625   3630

Lys Asn Glu Val Arg Ile His Ser Gly Ser Phe Gln Ser Gln Val
    3635   3640   3645

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Glu Leu  Ser Asn Asp Gln Glu  Lys Ala His Leu Asp  Ile Ala Gly
    3650             3655          3660

Ser Leu  Glu Gly His Leu Arg  Phe Leu Lys Asn Ile  Ile Leu Pro
    3665             3670          3675

Val Tyr  Asp Lys Ser Leu Trp  Asp Phe Leu Lys Leu  Asp Val Thr
    3680             3685          3690

Thr Ser  Ile Gly Arg Arg Gln  His Leu Arg Val Ser  Thr Ala Phe
    3695             3700          3705

Val Tyr  Thr Lys Asn Pro Asn  Gly Tyr Ser Phe Ser  Ile Pro Val
    3710             3715          3720

Lys Val  Leu Ala Asp Lys Phe  Ile Thr Pro Gly Leu  Lys Leu Asn
    3725             3730          3735

Asp Leu  Asn Ser Val Leu Val  Met Pro Thr Phe His  Val Pro Phe
    3740             3745          3750

Thr Asp  Leu Gln Val Pro Ser  Cys Lys Leu Asp Phe  Arg Glu Ile
    3755             3760          3765

Gln Ile  Tyr Lys Lys Leu Arg  Thr Ser Ser Phe Ala  Leu Asn Leu
    3770             3775          3780

Pro Thr  Leu Pro Glu Val Lys  Phe Pro Glu Val Asp  Val Leu Thr
    3785             3790          3795

Lys Tyr  Ser Gln Pro Glu Asp  Ser Leu Ile Pro Phe  Phe Glu Ile
    3800             3805          3810

Thr Val  Pro Glu Ser Gln Leu  Thr Val Ser Gln Phe  Thr Leu Pro
    3815             3820          3825

Lys Ser  Val Ser Asp Gly Ile  Ala Ala Leu Asp Leu  Asn Ala Val
    3830             3835          3840

Ala Asn  Lys Ile Ala Asp Phe  Glu Leu Pro Thr Ile  Ile Val Pro
    3845             3850          3855

Glu Gln  Thr Ile Glu Ile Pro  Ser Ile Lys Phe Ser  Val Pro Ala
    3860             3865          3870

Gly Ile  Val Ile Pro Ser Phe  Gln Ala Leu Thr Ala  Arg Phe Glu
```

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          3875                      3880                       3885

    Val Asp Ser Pro Val Tyr Asn  Ala Thr Trp Ser Ala  Ser Leu Lys
        3890                      3895                3900


    Asn Lys Ala Asp Tyr Val Glu  Thr Val Leu Asp Ser  Thr Cys Ser
        3905                      3910                3915


    Ser Thr Val Gln Phe Leu Glu  Tyr Glu Leu Asn Val  Leu Gly Thr
        3920                      3925                3930


    His Lys Ile Glu Asp Gly Thr  Leu Ala Ser Lys Thr  Lys Gly Thr
        3935                      3940                39 45


    Leu Ala His Arg Asp Phe Ser  Ala Glu Tyr Glu Glu  Asp Gly Lys
        3950                      3955                3960


    Phe Glu Gly Leu Gln Glu Trp  Glu Gly Lys Ala His  Leu Asn Ile
        3965                      3970                3975


    Lys Ser Pro Ala Phe Thr Asp  Leu His Leu Arg Tyr  Gln Lys Asp
        3980                      3985                3990


    Lys Lys Gly Ile Ser Thr Ser  Ala Ala Ser Pro Ala  Val Gly Thr
        3995                      4000                4005


    Val Gly Met Asp Met Asp Glu  Asp Asp Asp Phe Ser  Lys Trp Asn
        4010                      4015                4020


    Phe Tyr Tyr Ser Pro Gln Ser  Ser Pro Asp Lys Lys  Leu Thr Ile
        4025                      4030                4035


    Phe Lys Thr Glu Leu Arg Val  Arg Glu Ser Asp Glu  Glu Thr Gln
        4040                      4045                4050


    Ile Lys Val Asn Trp Glu Glu  Glu Ala Ala Ser Gly  Leu Leu Thr
        4055                      4060                4065


    Ser Leu Lys Asp Asn Val Pro  Lys Ala Thr Gly Val  Leu Tyr Asp
        4070                      4075                4080


    Tyr Val Asn Lys Tyr His Trp  Glu His Thr Gly Leu  Thr Leu Arg
        4085                      409 0               4095


    Glu Val Ser Ser Lys Leu Arg  Arg Asn Leu Gln Asn  Asn Ala Glu
        4100                      4105                4110
```

```
Trp Val  Tyr Gln Gly Ala Ile  Arg Gln Ile Asp Asp  Ile Asp Val
    4115             4120              4125

Arg Phe  Gln Lys Ala Ala Ser  Gly Thr Thr Gly Thr  Tyr Gln Glu
    4130             4135              4140

Trp Lys  Asp Lys Ala Gln Asn  Leu Tyr Gln Glu Leu  Leu Thr Gln
    4145             4150              4155

Glu Gly  Gln Ala Ser Phe Gln  Gly Leu Lys Asp Asn  Val Phe Asp
    4160             4165              4170

Gly Leu  Val Arg Val Thr Gln  Lys Phe His Met Lys  Val Lys His
    4175             4180              4185

Leu Ile  Asp Ser Leu Ile Asp  Phe Leu Asn Phe Pro  Arg Phe Gln
    4190             4195              4200

Phe Pro  Gly Lys Pro Gly Ile  Tyr Thr Arg Glu Glu  Leu Cys Thr
    4205             4210              4215

Met Phe  Ile Arg Glu Val Gly  Thr Val Leu Ser Gln  Val Tyr Ser
    4220             4225              4230

Lys Val  His Asn Gly Ser Glu  Ile Leu Phe Ser Tyr  Phe Gln Asp
    4235             4240              4245

Leu Val  Ile Thr Leu Pro Phe  Glu Leu Arg Lys His  Lys Leu Ile
    4250             4255              4260

Asp Val  Ile Ser Met Tyr Arg  Glu Leu Leu Lys Asp  Leu Ser Lys
    4265             4270              4275

Glu Ala  Gln Glu Val Phe Lys  Ala Ile Gln Ser Leu  Lys Thr Thr
    4280             4285              4290

Glu Val  Leu Arg Asn Leu Gln  Asp Leu Leu Gln Phe  Ile Phe Gln
    4295             4300              4305

Leu Ile  Glu Asp Asn Ile Lys  Gln Leu Lys Glu Met  Lys Phe Thr
    4310             4315              4320

Tyr Leu  Ile Asn Tyr Ile Gln  Asp Glu Ile Asn Thr  Ile Phe A sn
    4325             4330              4335
```

```
Asp Tyr Ile Pro Tyr Val Phe  Lys Leu Leu Lys Glu  Asn Leu Cys
    4340            4345              4350


Leu Asn Leu His Lys Phe Asn  Glu Phe Ile Gln Asn  Glu L eu Gln
    4355            4360              4365


Glu Ala Ser Gln Glu Leu Gln  Gln Ile His Gln Tyr  Ile Met Ala
    4370            4375              4380


Leu Arg Glu Glu Tyr Phe Asp  Pro Ser Ile Val Gly  T rp Thr Val
    4385            4390              4395


Lys Tyr Tyr Glu Leu Glu Glu  Lys Ile Val Ser Leu  Ile Lys Asn
    4400            4405              4410


Leu Leu Val Ala Leu Lys Asp  Phe His Ser Glu Tyr  Ile Val Ser
    4415            4420              4425


Ala Ser Asn Phe Thr Ser Gln  Leu Ser Ser Gln Val  Glu Gln Phe
    4430            4435              4440


Leu His Arg Asn Ile Gln Glu  Tyr Leu Ser Il e Leu  Thr Asp Pro
    4445            4450              4455


Asp Gly Lys Gly Lys Glu Lys  Ile Ala Glu Leu Ser  Ala Thr Ala
    4460            4465              4470


Gln Glu Ile Ile Lys Ser Gln  Ala Ile Al a Thr Lys  Lys Ile Ile
    4475            4480              4485


Ser Asp Tyr His Gln Gln Phe  Arg Tyr Lys Leu Gln  Asp Phe Ser
    4490            4495              4500


Asp Gln Leu Ser Asp Tyr Tyr  Glu Ly s Phe Ile Ala  Glu Ser Lys
    4505            4510              4515


Arg Leu Ile Asp Leu Ser Ile  Gln Asn Tyr His Thr  Phe Leu Ile
    4520            4525              4530


Tyr Ile Thr Glu Leu Leu Lys  Ly s Leu Gln Ser Thr  Thr Val Met
    4535            4540             ·4545


Asn Pro Tyr Met Lys Leu Ala  Pro Gly Glu Leu Thr  Ile Ile Leu
    4550            4555              4560
```

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<210>  2
<211>  317
<212>  PRT
<213>  Homo sapiens

<400>  2

Met Lys Val Leu Trp Ala Ala Leu Leu Val Thr Phe Leu Ala Gly Cys
1               5                   10                  15


Gln Ala Lys Val Glu Gln Ala Val Glu Thr Glu Pro Glu Pro Glu Leu
            20                  25                  30


Arg Gln Gln Thr Glu Trp Gln Ser Gly Gln Arg Trp Glu Leu Ala Leu
        35                  40                  45


Gly Arg Phe Trp Asp Tyr Leu Arg Trp Val Gln Thr Leu Ser Glu Gln
    50                  55                  60


Val Gln Glu Glu Leu Leu Ser Ser Gln Val Thr Gln Glu Leu Arg Ala
65                  70                  75                  80


Leu Met Asp Glu Thr Met Lys Glu Leu Lys Ala Tyr Lys Ser Glu Leu
                85                  90                  95


Glu Glu Gln Leu Thr Pro Val Ala Glu Glu Thr Arg Ala Arg Leu Ser
            100                 105                 110


Lys Glu Leu Gln Ala Ala Gln Ala Arg Leu Gly Ala Asp Met Glu Asp
        115                 120                 125


Val Cys Gly Arg Leu Val Gln Tyr Arg Gly Glu Val Gln Ala Met Leu
    130                 135                 140


Gly Gln Ser Thr Glu Glu Leu Arg Val Arg Leu Ala Ser His Le u Arg
145                 150                 155                 160


Lys Leu Arg Lys Arg Leu Leu Arg Asp Ala Asp Asp Leu Gln Lys Arg
                165                 170                 175


Leu Ala Val Tyr Gln Ala Gly Ala Arg Glu Gly Ala Gl u Arg Gly Leu
            180                 185                 190


Ser Ala Ile Arg Glu Arg Leu Gly Pro Leu Val Glu Gln Gly Arg Val
        195                 200                 205


Arg Ala Ala Thr Val Gly Ser Leu Ala Gly Gl n Pro Leu Gln Glu Arg
    210                 215                 220
```

```
Ala Gln Ala Trp Gly Glu Arg Leu Arg Ala Arg Met Glu Glu Met Gly
225             230             235             240

Ser Arg Thr Arg Asp Arg Leu Asp Glu Val Lys Glu Gln Val Ala Glu
            245             250             255

Val Arg Ala Lys Leu Glu Glu Gln Ala Gln Gln Ile Arg Leu Gln Ala
            260             265             270

Glu Ala Phe Gln Ala Arg Leu Lys Ser Trp Phe Glu Pro Leu Val Glu
        275             280             285

Asp Met Gln Arg Gln Trp Ala Gly Leu Val Glu Lys Val Gln Ala Ala
    290             295             300

Val Gly Thr Ser Ala Ala Pro Val Pro Ser Asp Asn His
305             310             315
```

```
<210>   3
<211>   11
<212>   PRT
<213>   synthetic construct

<400>   3

Glu Asn Phe Ala Gly Glu Ala Thr Leu Gln Arg
1               5               10
```